

IT IS CLAIMED:

1. An antibacterial compound consisting of a substantially uncharged antisense oligomer containing from 8 to 40 nucleotide subunits, including a targeting nucleic acid sequence at least 10 nucleotides in length which is complementary to a bacterial 16S or 23S rRNA nucleic acid sequence, wherein

each of said subunits comprises a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base in the bacterial nucleic acid sequence, and

10 adjacent subunits are joined by uncharged linkages selected from the group consisting of: uncharged phosphoramidate, phosphorodiamidate, carbonate, carbamate, amide, phosphotriester, alkyl phosphonate, siloxane, sulfone, sulfonamide, sulfamate, thioformacetyl, and methylene-N-methylhydroxylamino, or by charged linkages selected from the group consisting of phosphate, charged phosphoramidate and phosphorothioate, wherein the ratio of uncharged linkages to charged linkages in the oligomer is at least 4:1.

15 2. The compound of claim 1, wherein said oligomer is able to hybridize with the bacterial sequence at a  $T_m$  substantially greater than the  $T_m$  of a duplex composed of a corresponding DNA and the same bacterial sequence.

20 3. The compound of claim 1, wherein said oligomer is able to hybridize with the bacterial sequence at a  $T_m$  substantially greater than 37°C.

25 4. The compound of claim 1, wherein the oligomer is a morpholino oligomer.

5. The compound of claim 1, wherein the uncharged linkages are selected from the group consisting of the structures presented in Figures 2A through 2D.

30 6. The compound of claim 5, wherein each uncharged linkage is a phosphorodiamidate linkage as represented at Figure 2B, where  $X=NR_2$ , where R is hydrogen or methyl, Y=O, and Z=O.

7. The compound of claim 4, wherein each linkage is a phosphorodiamidate linkage as represented at Figure 2B, where  $X=NR_2$ , where R is hydrogen or methyl, Y=O, and Z=O.

8. The compound of claim 1, wherein wherein the ratio of uncharged linkages to charged linkages in the oligomer is at least 8:1.

5 9. The compound of claim 1, wherein the antisense oligomer has a length of from 12 to 25 subunits.

10 10. The compound of claim 7, having a length of 15 to 20 subunits.

11. The compound of claim 1, wherein the targeting sequence is selected from the group 10 consisting of SEQ ID NOs: 15, 16, and 21-25.

12. The compound of claim 1, where the targeting sequence is complementary to a Gram-positive bacterial 16S rRNA consensus sequence or a Gram-negative bacterial 16S rRNA consensus sequence.

15 13. The compound of claim 12, where the targeting sequence is selected from the group consisting of SEQ ID NOs: 27-30.

20 14. The compound of claim 1, wherein the targeting sequence is SEQ ID NO: 92.

15 15. A method of treating a bacterial infection in a human or mammalian animal subject, comprising

25 administering to the subject, in a pharmaceutically effective amount, a substantially uncharged antisense oligomer containing from 8 to 40 nucleotide subunits, including a targeting nucleic acid sequence at least 10 nucleotides in length which is complementary to a bacterial 16S or 23S rRNA nucleic acid sequence, wherein

each of said subunits comprises a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base in the bacterial nucleic acid sequence, and

30 adjacent subunits are joined by uncharged linkages selected from the group consisting of: uncharged phosphoramidate, phosphorodiamidate, carbonate, carbamate, amide, phosphotriester, alkyl phosphonate, siloxane, sulfone, sulfonamide, sulfamate, thioformacetyl, and methylene-N-methylhydroxylamino, or by charged linkages selected from the group consisting of phosphate, charged phosphoramidate and phosphorothioate, wherein the ratio of uncharged linkages to 35 charged linkages in the oligomer is at least 4:1.

16. The method of claim 15, wherein said oligomer is able to hybridize with the bacterial sequence at a  $T_m$  substantially greater than 37°C.

5 17. The method of claim 15, wherein the oligomer is a morpholino oligomer.

18. The method of claim 16, wherein the uncharged linkages are selected from the group consisting of the structures presented in Figures 2A through 2D.

10 19. The method of claim 18, wherein each uncharged linkage is a phosphorodiamidate linkage as represented at Figure 2B, where  $X=NR_2$ , where R is hydrogen or methyl, Y=O, and Z=O.

20. The method of claim 17, wherein each linkage is a phosphorodiamidate linkage as represented at Figure 2B, where  $X=NR_2$ , where R is hydrogen or methyl, Y=O, and Z=O.

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21. The method of claim 15, where the antisense oligomer has a length of from 12 to 25 bases.

22. The method of claim 17, wherein the oligomer has a length of from 15 to 20 bases.

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23. The method of claim 15, wherein the targeting sequence is selected from the group consisting of SEQ ID NOs: 15, 16 and 21-25.

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24. The method of claim 15, where the targeting sequence is complementary to a Gram-positive bacterial 16S rRNA consensus sequence or a Gram-negative bacterial 16S rRNA consensus sequence.

25. The method of claim 24, where the targeting sequence is selected from the group consisting of SEQ ID NOs:27-30.

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26. The method of claim 21, for use in treatment of an infection produced by *E. coli*, *Salmonella* *thyphimurium*, *Pseudomonas aeruginosa*, *Vibrio cholera*, *Neisseria gonorrhoea*, *Helicobacter pylori*, *Bartonella henselae*, *Hemophilis Influenza*, *Shigella dysenteriae*, *Staphylococcus aureus*, *Mycobacterium tuberculosis*, *Streptococcus pneumoniae*, *Treponema palladium* and *Chlamydia trachomatis*, where the antisense oligomer has a sequence selected from the group consisting of SEQ ID NOs: 21-25.

27. The method of claim 15, wherein the antisense oligomer is administered in an amount and manner effective to result in a peak blood concentration of at least 200-400 nM antisense oligomer.

5 28. The method of claim 15, for treating bacterial infections of the skin, wherein said administering is by a topical route.

29. The method of claim 12, for use in treating a bacterial respiratory infection, wherein said administering is by inhalation.

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30. A livestock and poultry food composition containing a food grain supplemented with a subtherapeutic amount of an antibacterial compound, said compound consisting of a substantially uncharged antisense oligomer containing from 8 to 40 nucleotide subunits, including a targeting nucleic acid sequence at least 10 nucleotides in length which is complementary to a bacterial 16S or 15 23S rRNA nucleic acid sequence, wherein

each of said subunits comprises a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base in the bacterial nucleic acid sequence, and adjacent subunits are joined by uncharged linkages selected from the group consisting of: uncharged phosphoramidate, phosphorodiamidate, carbonate, carbamate, amide, phosphotriester, alkyl phosphonate, siloxane, sulfone, sulfonamide, sulfamate, thioformacetyl, and 20 methylene-N-methylhydroxylamino, or by charged linkages selected from the group consisting of phosphate, charged phosphoramidate and phosphorothioate, wherein the ratio of uncharged linkages to charged linkages in the oligomer is at least 4:1.

25 31. The composition of claim 30, wherein the oligomer is a morpholino oligomer.

32. The composition of claim 31, wherein each linkage is a phosphorodiamidate linkage as represented at Figure 2B, where X=NR<sub>2</sub>, where R is hydrogen or methyl, Y=O, and Z=O.

30 33. The composition of claim 30, wherein the antisense oligomer has a length of from 12 to 25 bases.

34. The composition of claim 30, wherein the targeting sequence is selected from the group consisting of SEQ ID NOS: 15, 16, 21-25 and 27-30.

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